109

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,779	08/09/2001	Michael L. Roukes	049411-0204	5454

22428 7590 07/27/2006

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/927,779	Applicant(s) ROUKES ET AL.	
	Examiner Ann Y. Lam	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 08 May 2006.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,11-26,34-37,40,42,43,46,47,49,50 and 53* is/are pending in the application.

4a) Of the above claim(s) *6-10,33,38,39,41,44,45,48,51,52 and 54-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11-26,34-37,40,42,43,46,47,49,50 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

It is noted that claim 43 was inadvertantly placed under Group II (drawn to a resonator and a substrate biofunctionalized with a receptor) in the restriction requirement when it should have been placed under Group V (drawn to two resonators). This has been rectified. Because Applicant had elected Group II, claim 43 is deemed to be withdrawn as being directed to a non-elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 11-13, 15, 17-26, 34, 35, 37, 40, 42, 46, 47, 50, 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altmann et al., 6,545,492, in view of Thundat et al., 6,289,717.

As to claims 1, 34, 53, Altmann et al. disclose a molecular detector capable of detecting single-molecules in solution comprising:

a solution reservoir (col. 16, lines 4-8);

at least one biofunctionalized mechanical resonator disposed within the reservoir (col. 17, lines 29-40, “an oscillating cantilever”); and

a detector in signal communication with the at least one resonator for measuring a damping of resonance motion of the resonator in response to a molecular binding event on the resonator (col. 14, lines 50-60, which discloses detectors, and col. 17, lines 32-36, wherein the interactions between the cantilever and the sample lead to a dependency of the oscillating amplitude, which can be evaluated to obtain information about the interactions). Altmann et al. however do not teach that the resonator is on the nanometer scale.

Thundat et al., however, teach microcantilevers as small as 1 micrometer wide, 1 micrometer long, and 0.3 micrometers thick (column 3, lines 54-60), which would therefore be on the nanometer scale. Thundat et al. further teach that the resulting small size of the sensor require only minute concentrations of antigen to be used as the detecting molecule, allowing screening protocols to be developed for antigens or like detector molecules which are only available in limited supplies (column 7, lines 57-62).

Therefore, it would have been obvious to have microcantilevers as small as 1 micrometer wide, 1 micrometer long, and 0.3 micrometers thick as the resonator of Altmann et al., as suggested by Thundat et al., in order to obtain sensors that require only minute concentrations of antigen to be used as the detecting molecule, allowing screening protocols to be developed for antigens or like detector molecules which are only available in limited supplies.

As to claim 2, Altmann et al. disclose that the at least one resonator comprises a vibrational resonator ("vibrating cantilever", col. 17, lines 50-53).

As to claim 3, the vibrational resonator ("vibrating cantilever", col.17, line 50-53) of Altmann et al. has a triangular notch at the base (see fig. 2), and therefore would be a notched vibrational resonator.

As to claim 4, Altmann et al. disclose that the at least one resonator is biofunctionalized with a receptor (col. 16, lines 20-26).

As to claims 5, 42, Altmann et al. disclose that the device further comprises a substrate ("sample", on col. 16, lines 23-25) disposed within the reservoir and adjacent to the at least one resonator (col. 16, lines 4-10, fig.1), wherein the substrate is biofunctionalized with a ligand capable of molecular interaction with the receptor ("one could bind DNA to a sample surface.... and to a spherical probe attached to an AFM cantilever", col. 16, lines 23-27).

With respect to claim 11, Thundat et al. disclose that the microcantilever may be constructed of silicon or silicon dioxide (column 4, lines 1-5).

As to claim 12, Altmann et al. disclose that the detector is integral with the resonator (col. 14, lines 50-57, where piezo-electrical cantilevers that produces its own electrical signals for measurements of interactions with the sample is used).

As to claim 13, Altmann et al. disclose that the detector is a piezoresistive transducer (column 13, lines 58-61).

As to claim 15, Altmann et al. disclose that the detector is an optical detector (col. 14, lines 56-60).

With respect to claims 17, 35, Thundat et al. teach microcantilevers as small as 1 micrometer wide, 1 micrometer long, and 0.3 micrometers thick (column 3, lines 54-60).

As to claims 18-22, Altmann et al. do not disclose that the resonator has a resonance motion vacuum frequency between about 0.1 and 12 MHz (claim 18), nor a force constant between about 0.1mN/m and 1N/m (claim 19), nor a Reynolds number between about 0.001 and 2.0 (claim 20), nor a mass loading coefficient between about 0.3 and 11 (claim 21), nor a force sensitivity of about 8fN/√Hz or greater (claim 22).

However, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. In this case, Altmann et al. disclose the general conditions of the claims (see above with respect to claim 1), and the ranges recited in claims 18 through 22 relate to optimum or workable ranges and thus would only involve routine skill in the art according to *In re Aller.*

As to claims 23, Altmann et al. disclose that the resonator is biofunctionalized to detect a receptor/ligand interaction (col. 16, lines 18-21).

As to claims 24, Altmann et al. disclose that the resonator is biofunctionalized to detect DNA hybridization (col. 16, lines 23-28).

As to claim 25, Altmann et al. disclose that the resonator is biofunctionalized to detect a chemical bond (col.8, lines 58-63).

As to claim 26, Altmann et al. disclose that the resonator is biofunctionalized to detect protein unfolding (col. 8, lines 58-60).

As to claim 37, Altmann et al. disclose a solution reservoir (col. 16, lines 4-8); at least one biofunctionalized mechanical resonator disposed within the reservoir (col. 17, lines 29-40, "an oscillating cantilever"); a substrate ("sample", on col. 16, lines 23-25) disposed within the reservoir and adjacent to the at least one resonator (col. 16, lines 4-10, fig.1), wherein the substrate is biofunctionalized with a ligand capable of molecular interaction with the receptor ("one could bind DNA to a sample surface.... and to a spherical probe attached to an AFM cantilever", col. 16, lines 23-27); and a detector capable of measuring a mechanical displacement of the resonator (col. 17, lines 32-36, wherein the interactions between the cantilever and the sample lead to a dependency of the oscillating amplitude, which can be evaluated to obtain information about the interactions).

As to claims 40 and 50, Altmann et al. disclose that the substrate ("sample", on col. 16, lines 23-25) is disposed in the reservoir (fig.1).

As to claim 42, Altmann et al. disclose that the substrate is biofunctionalized with a ligand and the resonator is biofunctionalized with a receptor ("one could bind DNA to a sample surface.... and to a spherical probe attached to an AFM cantilever" col. 16, lines 23-27; "molecules bound to the AFM probe can be used as chemical sensors to detect forces between the molecules on the tip and target molecules on a surface... for example, the binding forces of individual ligand-receptor pairs" col. 16, lines 14-20).

As to claim 46, Altmann et al. disclose a driving element as claimed (see col. 17, lines 30-33, disclosing that the cantilever is externally driven to oscillate at a certain frequency.)

As to claim 47, Altmann et al. disclose that the device further comprises a substrate ("sample", on col. 16, lines 23-25) disposed within the reservoir and adjacent to the at least one resonator (col. 16, lines 4-10, fig.1), wherein the substrate is biofunctionalized with a ligand capable of molecular interaction with the receptor ("one could bind DNA to a sample surface.... and to a spherical probe attached to an AFM cantilever", col. 16, lines 23-27), and a detector in signal communication with the at least one resonator for measuring a mechanical displacement of the resonator (col. 17, lines 32-36, disclosing that the interactions between the cantilever and the sample lead to a dependency of the oscillating amplitude, which can be evaluated to obtain information about the interactions).

Claims 14, 36, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altmann et al., 6,545,492, in view of Thundat et al., 6,289,717, as applied to claim 13, and further in view of Chui et al., "Independent detection of vertical and lateral forces with a sidewall-implanted dual-axis piezoresistive cantilever", Applied Physics Letters, Vol. 72, Number 11, March 1998, pp. 1388-1390.

Altmann et al. in view of Thundat et al. teach a piezoresistive transducer, but do not teach that the transducer is made of p+doped silicon, as recited in claim 14, or that the transducer comprises a piezoresistive detector layer located on the resonator, as recited in claims 36, 49.

Chui et al., however, teach a cantilever with a piezoresistive boron doped (p doped) layer (page 1388, fig. 1) on a silicon layer (page 1389, left column). Chiu et al.

further teach that a piezoresistive boron layer provides high conductivity for detection of forces (see page. 1388, right column).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a silicon p doped piezoresistive cantilever as taught by Chui et al. in the Altmann et al. -Thundat et al. invention because Chui et al. teach that a piezoresistive sensor that is p doped provides the advantage of high conductivity for detection of forces.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Altmann et al., 6,545,492, in view of Thundat et al., 6,289,717, as applied to claim 1, and further in view of Lee et al., 5,807,758.

Altmann et al. in view of Thundat et al. teach a detector, as discussed above, but do not teach a lock-in detector.

Lee et al., however, teach a lock-in detector comprising piezoresistive elements directed through a pair of high pass filters and then into a lock-in amplifier (column 9, lines 11-25). Lee et al. further teach that lock-in techniques may be used to further reduce or eliminate noise by narrowing the bandwidth of the system (column 8, lines 65-67).

Therefore, it would have been obvious to one of ordinary skill in the art to utilize the detector of Altmann et al. and Thundat et al. as a lock-in detector, as suggested by Lee et al., for the advantages of further reducing or eliminating noise by narrowing the bandwidth of the system.

Response to Arguments

Applicant's arguments with respect to claims 1-5, 11-26, 34-37, 40, 42, 46, 47, 49, 50, 53 have been considered but are moot in view of the new ground(s) of rejection.

Rejections Withdrawn

Applicant's arguments, filed May 8, 2006, with respect to the rejections under 35 U.S.C. 112, second paragraph, have been fully considered and are persuasive. The rejection of claims 1-5, 11-26, 34-37, 40, 42, 43, 46, 47, 49, 50, 53 under 35 U.S.C. 112, second paragraph, has been withdrawn.

Applicant's arguments on page 13-15, filed May 8, 2006, with respect to the rejections of claims 1-5, 11-26, 34-37, 40, 42, 43, 46, 47, 49, 50 and 53 under 35 U.S.C. 102(e) and under 35 U.S.C. 103(a) have been fully considered and are persuasive. The rejections of claims 1-5, 11-26, 34-37, 40, 42, 43, 46, 47, 49, 50, 53 under 35 U.S.C. 102(e) and under 35 U.S.C. 103(a) have been withdrawn. New grounds of rejections are made above however.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ann Lam 7/23/06